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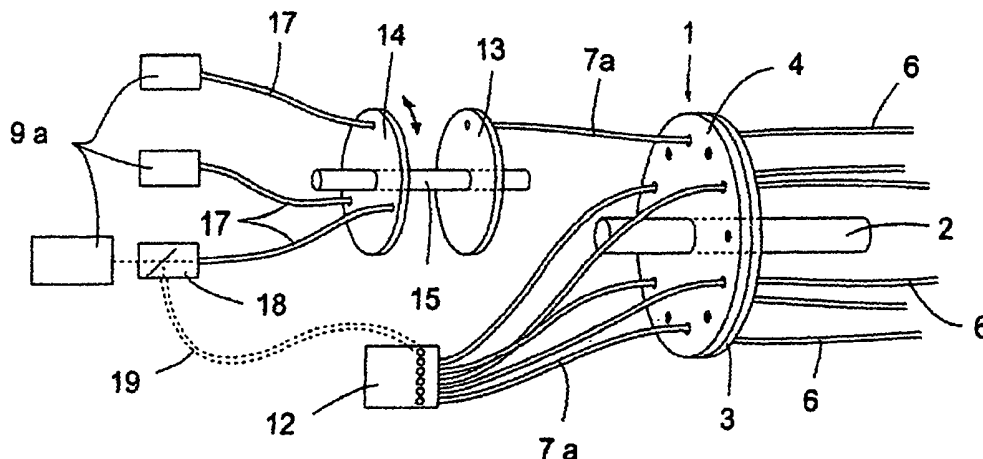
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(54) Title: **THERAPY AND DIAGNOSIS SYSTEM AND METHOD WITH DISTRIBUTOR FOR DISTRIBUTION OF RADI-
ATION**



(57) Abstract: A system and method for interactive, interstitial photodynamic and/or photothermal tumour therapy, said system comprising a distributor (1) for distribution of radiation from at least one radiation source (9a, 9b) to a reaction site (8), or from the reaction site (8) to at least one radiation sensor (12). A plurality of first radiation conductors (6, 6') are arranged for conduction of radiation to and from the reaction site (8) and a plurality of second radiation conductors (7, 7a, 7a', 7b) are arranged for emitting radiation from the radiation source (9a, 9b) and/or conduction of radiation to the radiation sensor (12). The distributor comprises two plane discs (3, 4), mounted abutting each other, one being fixed and the other turnable relative the first, each disc having holes arranged equally separated on a circle line; the number of holes in the turnable disc being a multiple of the number of holes in the fixed disc. One end of the first radiation conductors (6, 6') are fixed in the holes of the fixed disc (3) and one end of the second radiation conductors (7, 7a, 7a', 7b) are fixed in the holes of the turnable disc.



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**THERAPY AND DIAGNOSIS SYSTEM AND METHOD WITH DISTRIBUTOR
FOR DISTRIBUTION OF RADIATION**

The invention relates to a system and a method for
5 photodynamic therapy and/or photothermal therapy and/or
diagnosis of a site on and/or in a body, wherein radiation
is conducted to the site for reaction with the radiation,
wherein the system comprises a distributor of radiation
from at least one source of radiation to a reaction site,
10 and from the reaction site to at least one radiation
sensor, respectively, and wherein the reaction site pre-
ferably is a tumour site.

Within the field of medical therapy of tumour
diseases, a plurality of treatment modalities has been
15 developed for the treatment of malignant tumour diseases,
e.g. a tumefaction. Operation, cytostatics treatment,
treatment with ionising radiation (gamma or particle
radiation), isotope therapy and brachy therapy employing
radioactive needles are examples of common treatment
20 modalities. In spite of great progress within therapy, the
tumour diseases continue to account for much human suffer-
ing, and are responsible for a high percentage of deaths in
Western countries. A relatively new treatment modality,
photodynamic therapy, commonly abbreviated PDT, provides an
25 interesting complement or alternative in the treatment
field. A tumour-seeking agent, normally referred to as a
sensitiser, is administered to the body intravenously,
orally or topically. It accumulates in malignant tumours to
a higher extent than in the surrounding healthy tissue. The
30 tumour area is then irradiated with non-thermal red light,
normally from a laser, leading to excitation of the sensi-

tiser to a more energetic state. Through energy transfer from the activated sensitiser to the oxygen molecules of the tissue, the oxygen is transferred from its normal triplet state to the excited singlet state. Singlet oxygen
5 is known to be particularly toxic to tissue; cells are eradicated and the tissue goes in necrosis. Because of the localisation of the sensitiser to tumour cells a unique selectivity is obtained, where surrounding healthy tissue is spared. The initial clinical experience, using in
10 particular haematoporphyrin derivative (HPD) and delta amino levulinic acid (ALA) are good.

Sensitisers also exhibit a further useful property; to yield a characteristic red fluorescence signal when the substance is excited with violet or ultraviolet radiation.
15 This signal clearly appears in contrast to the autofluorescence of the tissue and can be used to localise tumours and for quantifying the size of the uptake of the sensitiser in the tissue.

The limited penetration in the tissue of the activating red radiation is a big drawback of PDT. The result is
20 that only tumours up to about 5 mm thickness can be treated by surface irradiation. In order to treat thicker and deep-lying tumours, interstitial PDT (IPDT) can be utilised. Here, light-conducting optical fibres are brought into the
25 tumour using, e.g. a syringe needle, in the lumen of which a fibre has been placed.

In order to achieve an efficient treatment, several fibres have been used to ascertain that all tumour cells are subjected to a sufficient dose of light so that the
30 toxic singlet state is obtained. It has been shown to be achievable to perform dose calculations of the absorptive

and scattering properties of the tissue. E.g., in the Swedish patent SE 503 408 an IPDT system is described, where six fibres are used for treatment as well as for measurement of the light flux which reaches a given fibre
5 in the penetration through the tissue from the other fibres. In this way an improved calculation of the correct light dose can be achieved for all parts of the tumour.

In the equipment described in SE 503 408 the light from a single laser is divided up in six different parts
10 using a beamsplitter system comprising a large number of components. The light is then focused into each of the six individual treatment fibres. One fibre is used as a transmitter while the other fibres are used as receivers of radiation penetrating the tissue. For light measurement
15 light detectors are swung into the beam path which thus is blocked, and the weak light, which originates from the fibres that collected the light which is administered to the tissue, is measured.

However, such open beam paths result in a strongly
20 lossy beamsplitting and the resulting losses of light drastically impair the light distribution as well as the light measurement. Furthermore, such a system must often be adjusted optically, which is also an important consideration in connection with clinical treatments.

25 The purpose of the invention is to eliminate the drawbacks mentioned above, which can be achieved by assigning to the system characteristics according to claim 1, wherein a very practical and efficient implementation of interactive IPDT is achieved in that different optical measurements for diagnostics and dosimetry can be performed in an
30 integrated and simple way. An important application of the

invention is interactive, interstitial photodynamic therapy, and/or interactive photothermal tumour therapy.

In order to more closely explain the invention a number of embodiments of the invention will be described in the following with reference to the figures, wherein

FIG 1 is a schematic perspective view of a first embodiment of the system according to the invention, wherein light conductors arranged in said invention are interstitially inserted in a tumour,

FIG 2 is a view similar to FIG 1, where the discs of the distributor are brought apart,

FIG 3 is a planar view from above of the turnable distributor disc with holes arranged in said disc,

FIG 4 is a fragmentary cross section view of the turnable disc of said distributor, wherein a spring-loaded ball is provided,

FIG 5 is a schematic perspective view illustrating the use of the system according to the invention with the distributor in the mode of tumour diagnostics,

FIG 6 is a view similar to FIG 5 and FIG 2, where two distributors are arranged on the same single axis, and

FIG 7 is a schematic perspective view illustrating the use of the system according to the invention, with the distributor in the mode of photodynamic treatment of a tumour.

A preferred embodiment of the distributor of the system according to the invention is now described with reference to FIG 1-4. The distributor 1 comprises two flat and in proximity lying discs made of, e.g. 1 cm thick steel. The discs are hereby arranged on an axis 2, wherein one of the discs is a fixed disc 3 and the other one is a turnable

disc 4. The discs 3 and 4 are abutting against each other in FIG 1 and separated from each other in FIG 2.

Evenly distributed holes 5 lying on a circle are arranged in both discs (FIG 3) for fixation of radiation
5 conductors 6, 7. Preferably the diameter of the holes is 0.3 - 0.7 mm. In order to attain a high precision, allowing the light conductors to be arranged exactly face to face, the holes of the two discs can be drilled together, maybe with a centring tube. Then the common axis 2 is utilised.
10 It is thus possible to achieve a very high precision when making the series of holes.

By employing discs drilled together, radiation conductors can be fixed in said discs, wherein an extra, thinner disc then can be turned slightly, preferably
15 spring-loaded, so that all light conductors are simultaneously pinched in their positions without the need for any glue or other fixation means. Alternatively, the diameter of the holes is made larger than the diameter of the light conductors, wherein the holes can be dressed with an appropriate piece of tubing, or the ends of the light conductors
20 can be supplied with a fitted hose. Alternatively, the ends of the light conductors can be flared or flanged into the holes.

Preferably the light conductors are optical fibres,
25 wherein different types of hoses or flexible tubes containing a light-conducting material are included. The light conductors should have such a length and be arranged in such a way that the turnable disc 4 can be turned without problems a full turn (360 degrees). The direction of movement can be reversed to avoid the light conductors forming
30 a spiral.

According to the invention a plurality of first light conductors 6 in a system are arranged in the fixed disc 3 for conduction of radiation to and from a reaction site 8. By a reaction site we in the present context mean a site
5 where photodynamically active compounds will react in a tumour when subject to therapy. E.g., by being forwarded through the lumen of injection needles which are placed in the tumour, these radiation conductors 6 are then fixed in the reaction site 8. Then the radiation conductors are
10 moved forward to arrive outside the distal end of the needle. The same light conductor 6 is used all the time for integrated diagnostics and dosimetry, to avoid that the patient be subjected to multiple pricks.

The holes 6 in the fixed disc 3 as well as in the
15 turnable disc 4 are arranged on a circular line, wherein the circle radius on one disc equals the circle radius on the other disc. The holes on one disc are equally distributed along the circle line with an angular separation $v_1 = (360/n_1)$ degrees, where n_1 equals the number of holes,
20 and the holes of the other disc are equally distributed along the circle line with an angular separation v_2 equaling $(360/n_2)$ degrees. The first ends of the first radiation conductors 6 are fixed in the holes of the fixed disc 3, and first ends of the second radiation conductors 7 are
25 fixed in the holes of the turnable disc 4. In order to make the holes, and thereby the radiation conductors in both discs connectable to each other in different constellations by turning of the turnable disc 4, n_2 is selected to be a multiple of n_1 , in such a way that n_2 is obtained as an
30 integer larger or equal to 1. Suitably the number of holes in the fixed disc is chosen from two to more than six.

Preferably six holes are arranged in the fixed disc 3 and twelve holes are arranged in the turnable disc 4. With six first radiation conductors 6 the angular separation will accordingly become 60 degrees in the fixed disc 3 and
5 with twelve holes arranged in the turnable disc 4 the angular separation will become 30 degrees for the second radiation conductors 7.

In order to facilitate the comprehension of the invention the following description of a preferred embodiment of
10 the distributor of the system according to the invention relates to six first radiation conductors 6 arranged in the fixed disc 3 for conduction of radiation to and from the reaction site 8.

Thus, the turnable disc 4, as well as the fixed disc
15 3, have six holes 5 for corresponding second radiation conductors 7, and, in addition, six further holes for second radiation conductors 7. All these radiation conductors 7 can release radiation to the reaction site 8 and receive radiation from said site. Thus, several spectra can
20 be recorded and read out simultaneously.

By turning the turnable disc 4 the first and the second radiation conductors become connectable to each other in different constellations. An exact positioning of the opposing radiation conductors in the distributor 1 is
25 facilitated by arranging means for stopping the turnable disc 4 in pre-determined angular positions. E.g., grooves 10 can be arranged in the axis 2 for catching a spring-loaded ball 11 arranged in the turnable disc 4 (FIG 4).

In order to allow a fast and efficient switching
30 between a diagnostic mode and a therapeutic mode, every second of the second light conductors of the distributor 1

according to the invention, are divided into a first and into a second series. Both series of holes are arranged on the same circle, but displaced by 30 degrees with regard to each other. A specific light conductor 7a' in the first series of every other second light conductor is arranged for emitting radiation from at least one radiation source 9a. The other, non specific radiation conductors 7a in the first series of second radiation conductors are arranged for conduction of radiation to at least one radiation sensor 12. The second series of every other second radiation conductor 7b is for therapeutical purposes arranged to emit radiation to the reaction site 8 from at least one radiation source 9b.

In the preferred embodiment of the invention, the radiation conductors are optical fibres, which in the distributor 1 shown in FIG 1 and 2 are connected to the fixed disc 3 as well as the turnable disc 4. Out of the fibres, which are connected to the turnable disc 4, six fibres can be used for diagnostic purposes and six can be used of therapeutical purposes. However, in the diagnostic mode, from one to more than three modalities can be employed.

With reference to FIG 5-7 only the presently described radiation conductors which are coupled to a turnable disc are for clarifying purposes shown; the other radiation conductors are not shown although they are coupled to said disc.

By turning the turnable disc 5 by 30 degrees the fibres 6 which are optically coupled to the tissue of the patient can be employed for therapy as well as diagnostics and measurements. One out of every second radiation con-

ductor 7 is in the diagnostic mode connected to different radiation sources for diagnostics, while the other five radiation conductors receive signals, which are related to the interaction of these radiation sources with the tissue.

5 Since intensity as well as spectral resolution is of interest, the distal ends of these five radiation conductors are arranged in a slit-like arrangement so that they overlap the entrance slit and/or constitute the entrance slit of the radiation sensor 12, which is a compact
10 spectrometer and is supplied with a two-dimensional detector array. The recording range of the spectrometer is preferably within the range 400 to 900 nm. Each of the radiation conductors 7a can of course be connected to an individual radiation detector 12 in the form of a spectrometer
15 or another type of detector, e.g. a compact integrated spectrometer.

 With reference to FIG 5 the specific radiation conductor 7a' is connected to an arrangement similar to the distributor 1, which comprises a second fixed disc 13 and a
20 second turnable disc 14 which are arranged on a common axis 15. All fixed and turnable discs can also be arranged on one single axis as is shown in FIG 6. A more compact and robust construction is obtained in this way.

 More specifically the radiation conductor 7a' is
25 arranged in a single hole on the second fixed disc 13. Further light conductors 17 are arranged on a circle in said second turnable disc 14; in this case three conductors which are connected to different radiation sources 9a, and which each are connectable to the radiation conductor 7a'
30 and further on to the different first radiation conductors 6.

Preferably the radiation source 9a is a laser of the same wavelength as the one utilised for the laser irradiation for photodynamic tumour therapy, but of substantially lower output power. Suitable filters can be arranged on the
5 second turnable disc 14, to be turned into the light path of the radiation sensor 12 in order to secure that the correct dynamic range is utilised for all measurement tasks.

Certain of the radiation sources 9a are utilised in order to study how radiation (light) of the corresponding
10 wavelength is penetrating through the tissue of the tumour. When light from a radiation source 9a is transmitted through the particular radiation conductor 7a' via the discs 14, 13, 4, 3 into the tissue, one of the first radiation conductors 6, which is the one opposing the radiation
15 conductor 6' in the distributor 1, will function as a transmitter in the tumour, and the other five radiation conductors 6 in the tumour will act as receivers and collect the diffuse flux of light reaching them. The light collected is again conducted via the discs 3, 4, 13, 14 to
20 the radiation sensor 12 and five different light intensities can be recorded on the detector array.

When the turnable disc 4 is turned by 60 degrees, the next radiation conductor 6 to the patient will get the role as transmitter, and the five others become the receivers
25 for a new light distribution. After four further turns of the turnable disc 4, each by 60 degrees to the following radiation conductor 6 in the patient, light flux data for all remaining combinations of transmitters/receivers have been recorded. Thus, in total $6 \times 5 = 30$ measurement values
30 are obtained and can be used as input data for a tomograph-

ic modelling of the optical dose build up in the different parts of the tumour during the course of the treatment.

As an alternative to a specific wavelength, radiation from a white light source can be coupled into the particular light conductor 7a'. On passage through the tissue to the receiving light conductor 6 in the patient, the well-defined spectral distribution of the radiation source 9a will be modified by the tissue absorption. Then, oxygenated blood yields a different signature than non oxygenated blood, allowing a tomographic determination of the oxygen distribution utilising the thirty different spectral distributions which are read out, five spectra at a time in the six possible different constellations on rotation of the turnable disc 4 during a diagnostic investigation. Such a determination of the oxygenation in the tumour is important, since the PDT process requires access to oxygen in the tissue.

Finally, a light source for blue/violet or ultraviolet light, e.g. a laser, can be coupled to the particular radiation conductor 7a'. Then fluorescence is induced in the tissue, and a sensitiser administered to the tissue displays a characteristic red fluorescence distribution in the red/near-infrared spectral region. The strength of the corresponding signal allows a quantification of the concentration of the sensitiser in the tissue.

Since the short wavelength light has a very low penetration into the tissue, the induced fluorescence must be measured locally at the tip of the radiation conductor. For this task there is in this case for the corresponding radiation source 9a at the distal end of the particular radiation conductor 7a' a beamsplitter 18, connected via the

radiation conductor 18 and which is preferably dichroitic, transmitting the exciting light but reflecting the red-shifted fluorescence light. This reflected light is focused into the distal end of a conveying radiation conductor 19, the other end of which is connected to the radiation sensor 12, which records the fluorescence light distribution. A suitable self-contained fluorosensor is described in Rev. Sci. Instr. **71**, 3004 (2000).

By rotating the turnable disc 4, the fluorescence which is proportional to the concentration of the sensitiser, can be measured sequentially at the tips of the six radiation conductors. Since the sensitiser is bleached by the strong red treatment light, being particularly strong just around the tip of the radiation conductor 6', it is essential to make this measurement before the start of the treatment.

If the tips of the radiation conductors 6 in addition are treated with a material, the fluorescence properties of which are temperature dependent, sharp fluorescence lines are obtained upon excitation, and the intensity of the lines and their relative strength depend on the temperature of the tip of the radiation conductor 6' being employed for treatment. Examples of such materials are salts of the transition metals or the rare earth metals. Thus also the temperature can be measured at the six positions of the six radiation conductors, one at a time. The measured temperatures can be utilised to find out if blood coagulation with an associated light attenuation has occurred at the tip of the radiation conductor 6 and for studies regarding the utilisation of possible synergy effects between PDT and thermal interaction. Since the lines obtained are sharp,

they can be lifted off the more broad-banded fluorescence distribution from the tissue.

The concentration of the sensitiser can for certain substances be measured in an alternative way. Then the red
5 light used for the light propagation studies is used to induce near-infrared fluorescence. This fluorescence penetrates through the tissue to the tips of the receiving radiation conductors 6, and are displayed simultaneously as spectra obtained in the radiation sensor 12. A tomographic
10 calculation of the concentration distribution can be performed based on in total thirty measurement values.

After diagnostic measurements and calculations have been performed, the fibres 6 optically coupled to the tissue of the patients can be utilised for therapy by rotation
15 of the turnable disc 4 by 30 degrees. Referring to FIG 7, the second series of every other second radiation conductor 7b is utilised, now connected to the opposing radiation conductors 6 via the distributor 1. Each of the six radiation conductors 7b is connected to an individual second
20 radiation source 9b, which preferably is a laser source with a wavelength which is adapted to the absorption band of the sensitiser. At the photodynamic tumour treatment a dye laser or a diode laser is preferably used, with a wavelength which is selected with regard to the sensitiser
25 employed. For Photofrin[®] the wavelength is 630 nm, for δ amino levulinic acid (ALA) it is 635 and for phthalocyanines it is around 670 nm. The individual lasers are regulated during the treatment to a desirable individual output power. If desired, they may have built-in monitoring
30 detectors.

The therapeutical treatment can be interrupted and new diagnostic data can be processed in an interactive method till an optimal treatment has been reached. This method can include synergy between PDT and hyperthermia, where an in-
5 creased temperature is reached at increased fluxes of laser radiation. The whole process is controlled using a computer, which does not only perform all the calculations but also is utilised for regulation.

CLAIMS

1. A system for interactive interstitial photodynamic
tumour therapy and/or photothermal tumour therapy and/or
5 tumour diagnosis, comprising at least one radiation source
(9a, 9b), at least one radiation sensor (12) and a radia-
tion conductor (6, 6') which are brought to a tumour site
(8), wherein the radiation conductor is in use employed as
a transmitter and/or a receiver for conduction of radiation
10 to and/or from the tumour site (8) for diagnosis and thera-
py of a tumour at the tumour site (8),

characterised by a distributor (1) for distribu-
tion of radiation from at least one radiation source (9a,
9b) to the tumour site (8), and from the tumour site (8) to
15 at least one radiation sensor (12), wherein the distributor
(1) comprises

a plurality of first radiation conductors (6, 6')
arranged for conducting radiation to and from the tumour
site (8),

20 a plurality of second radiation conductors (7,
7a', 7a'', 7b) arranged for delivering radiation from the
radiation source (9a, 9b) and/or conduction of radiation to
the radiation sensor (12),

two flat discs (3,4) abutting against each other,
25 wherein a first of said discs is fixed (3) and the second
of said discs is turnable (4) relatively to the other disc,

each disc has holes (5) arranged on a circular
line, wherein the circle radius on one disc equals the
circle radius on the other disc and where the holes in one
30 disc are equally distributed on the circle line with an
angular separation of $v_1 = (360/n_1)$ degrees, n_1 being the

number of holes, and the holes in the other disc are
equally distributed on the circle line with an angular
separation of $v_2 = (360/n_2)$ degrees, wherein $n_2 = m \times n_1$, and
wherein m is a multiple, which yields n_2 as an integer ≥ 1 ,
5 and

wherein the first ends of the first radiation
conductors (6, 6') are fixed in the holes of the fixed disc
(3) and first ends of the other radiation conductors (7,
7a, 7a', 7b) are fixed in the holes of the turnable disc
10 (4), whereby the first and the second radiation conductors
by rotation of the turnable disc are connectable to each
other in different constellations.

2. A system according to claim 1, **characterised**
by n_1 being the number of holes in the fixed disc (3) of
15 the distributor (1), $n_1 = 6$ and $m = 2$, yielding $n_2 = 12$
holes in the turnable disc (4) of the distributor (1).

3. A system according to claim 1 or 2, **character-**
ised by every other second radiation conductor (7) being
part of a first series of second radiation conductors and
20 that a radiation conductor (7a') in said first series of
second radiation conductors being arranged for emitting
radiation from the radiation source (9a) and the other
radiation conductors (7a) in said first series of second
radiation conductors being arranged for conduction of
25 radiation to the radiation sensor (12).

4. A system according to claim 3, **characterised**
by the radiation source (9a) being a light source for
white, red, blue/violet or ultraviolet light.

5. A system according to claim 4, **characterised**
30 by the light source comprising a beamsplitter (18).

6. A system according to claim 5, **characterised** by a transferring radiation conductor (19) being arranged between the dichroic beamsplitter (18) and the radiation sensor (12).

5 7. A system according to claim 4, **characterised** by the first radiation conductors (6, 6') second ends being treated by a material with temperature sensitive fluorescence emission.

8. A system according to any of the claims 1-7,
10 **characterised** by the radiation sensor (12) being a spectrometer with a two-dimensional detector array and the other ends of said other radiation conductors (7a) of said first series of second radiation conductors being arranged in the entrance slit of the spectrometer.

15 9. A system according to claim 1 or 2, **characterised** by every second other radiation conductor (7) being part of a second series of second radiation conductors arranged for emission of radiation from the radiation source (9b).

20 10. A system according to any of the claims 1-9, **characterised** by the radiation source (9a, 9b) being a light source for coherent light of a single fixed wavelength.

11. A system according to claim 1, **characterised**
25 by the distributor including means (10,11) arranged for locking the turnable disc (4) into pre-determined angular positions.

12. A system according to claims 1-11, **characterised**
30 by the radiation conductors (6, 6', 7, 7b) being optical fibres.

13. A system according to claims 4-6, **characterised** by fluorescence being recorded through the same radiation conductor (6') as the one transmitting radiation to the tumour site (8),

5 14. A system according to claim 7, **characterised** in that for interactive photodynamic therapy one or several of the radiation conductors (6, 6') which are treated with the material with a temperature sensitive fluorescence emission are measuring the temperature at the tumour site
10 (8),

that the radiation which is sent to the tumour site (8) heats the tumour site (8),

that the intensity of the radiation is controlled by the measured temperature in order to regulate the temperature of the tumour site (8) at the individual radiation
15 conductors (6, 6').

15. A method for interactive interstitial photodynamic tumour therapy and/or photothermal tumour therapy and/or tumour diagnosis, wherein at least one radiation
20 sensor (12) and radiation conductor (6, 6') is connected to a tumour site (8) and the radiation conductor is used as a transmitter and/or a receiver for conduction of radiation to and /or from a tumour site (8) for diagnosis and therapy of a tumour at the tumour site (8),

25 **characterised** in that the switching between tumour therapy and tumour diagnostics is achieved in an automatised way, and

that the results from the diagnostics control the therapy process by regulating a therapeutical radiation
30 intensity depending on the results of the diagnostics until

an optimal treatment of the tumour site (8) has been achieved.

16. A method according to claim 15, **characterised** in that switching between tumour diagnostics and tumour
5 therapy is achieved by rotating a turnable disc (4) in an optical distributor, such that different arrangements of radiation conductors and/or radiation sources and/or radiation sensors are connected to the radiation conductors (6, 6').

10 17. A method according to claim 16, **characterised** by alternately utilising interactive interstitial photodynamic tumour therapy, photothermal tumour therapy using hyperthermia, and tumour diagnostics during the same occasion of treatment of said tumour site (8).

15

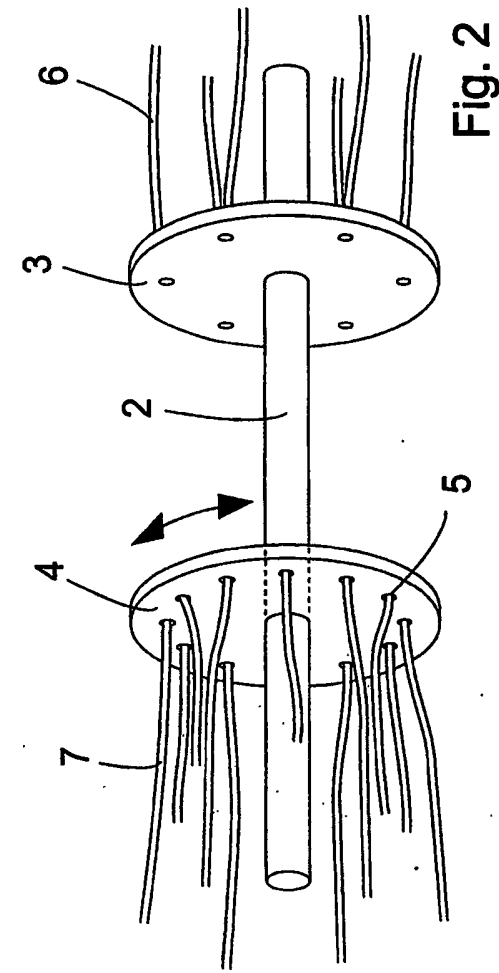


Fig. 2

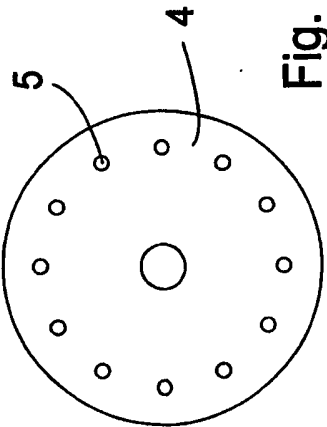


Fig. 3

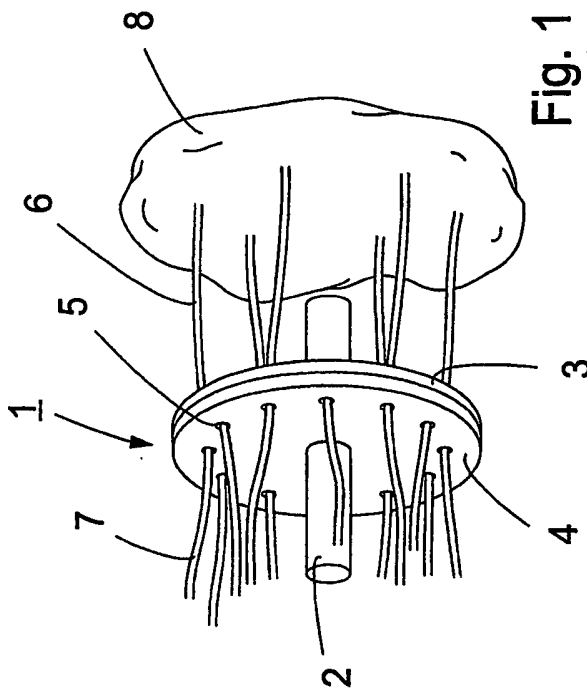


Fig. 1

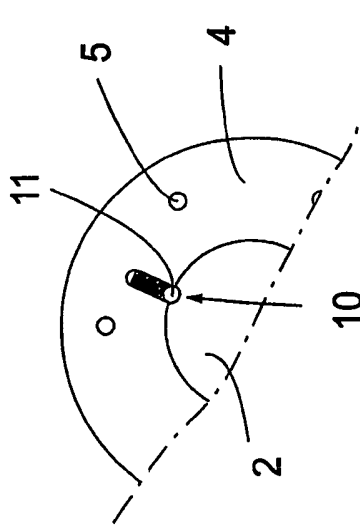
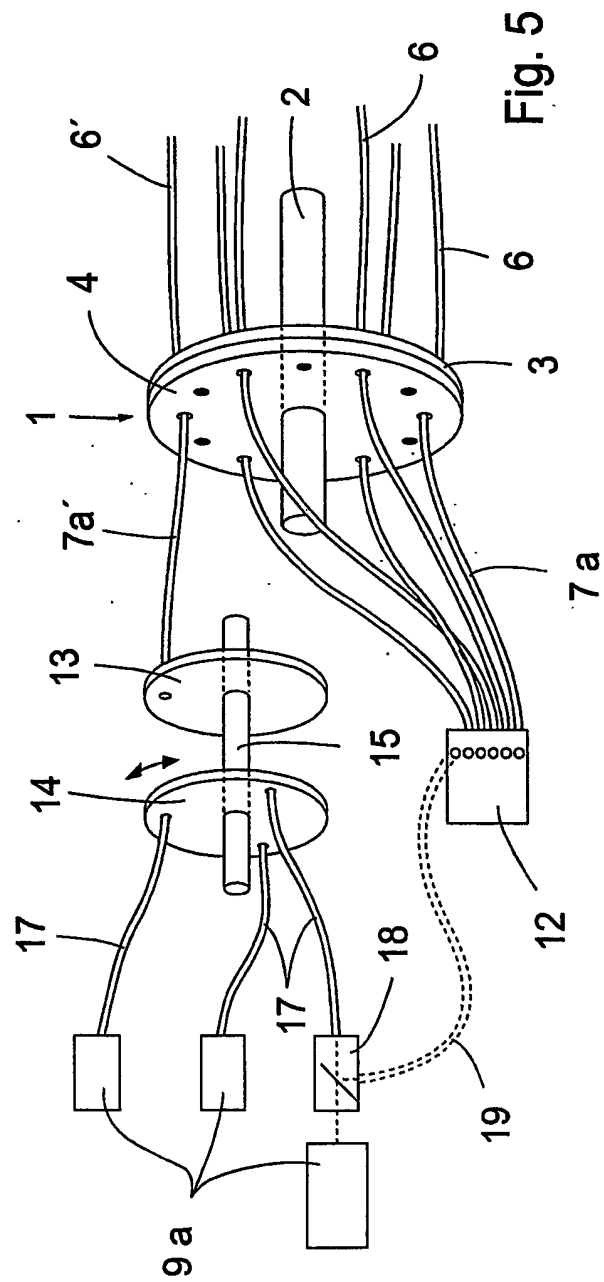
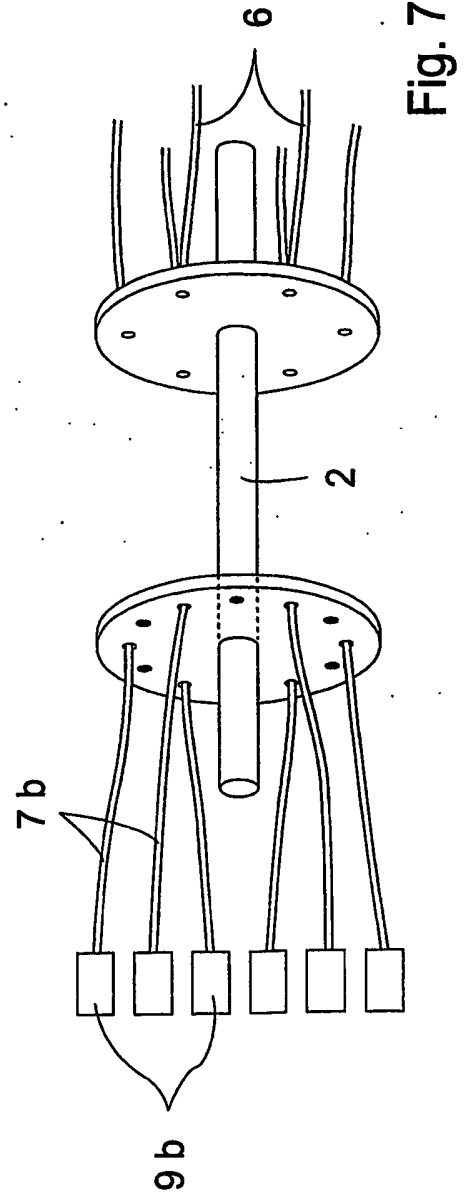
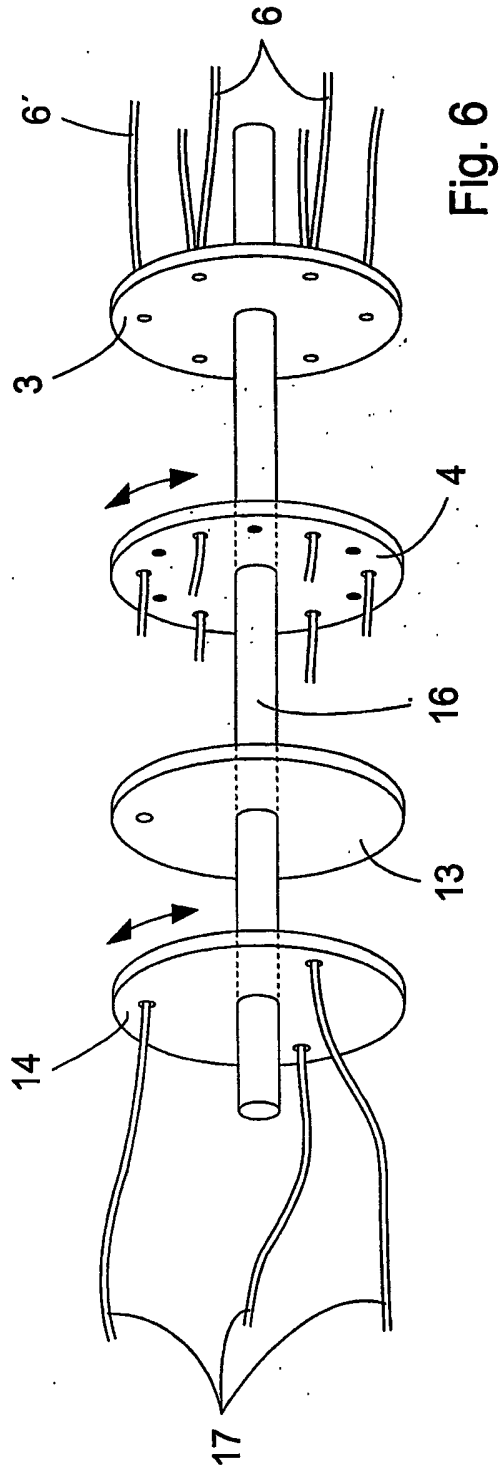


Fig. 4





A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61B5/00 A61B5/22 A61N5/06 G02B26/08

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61B A61N G02B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 195 375 A (MASSACHUSETTS INST TECHNOLOGY) 24 September 1986 (1986-09-24) the whole document	1-17
A	--- PATENT ABSTRACTS OF JAPAN vol. 012, no. 280 (P-739), 2 August 1988 (1988-08-02) & JP 63 060421 A (FUJIKURA LTD), 16 March 1988 (1988-03-16) abstract	1-3,12, 13
A	--- PATENT ABSTRACTS OF JAPAN vol. 017, no. 197 (P-1523), 16 April 1993 (1993-04-16) & JP 04 343317 A (FURUKAWA ELECTRIC CO LTD:THE), 30 November 1992 (1992-11-30) abstract -----	1-3,11

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

4 March 2003

Date of mailing of the international search report

27. 03. 2003

Name and mailing address of the ISA

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Authorized officer

BO GUSTAVSSON/JA A

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: **15-17**
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Claims Nos.: 15-17

Claims 15-17 relate to therapeutic methods practised on the human or animal body, namely methods for tumour therapy and/or diagnosis. Thus, the International Searching Authority is not required to carry out an international search for these claims (PCT Rule 39.1(iv)). Nevertheless, an International Search has been executed for claims 15-17.

INTERNATIONAL SEARCH REPORT

PCT/SE 02/02050

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
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